

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE
in its capacity as elected Office

Date of mailing (day/month/year) 22 June 2001 (22.06.01)	
International application No. PCT/US00/26949	Applicant's or agent's file reference P51032
International filing date (day/month/year) 29 September 2000 (29.09.00)	Priority date (day/month/year) 29 September 1999 (29.09.99)
Applicant BRIAND, Jacques	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

01 March 2001 (01.03.01)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Olivia TEFY Telephone No.: (41-22) 338.83.38
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/26949

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : G01N 33/53, 33/557, 33/566, 33/567, 24/00; G01R 33/035
US CL : 435/7.1; 436/501, 504, 517, 173; 505/844

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/7.1; 436/501, 504, 517, 173; 505/844

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WEST, STN (CAPLUS, SciSearch)

Terms: NMR, nuclear magnetic resonance, one/two dimensional (1D, 2D), screen?, interact, bind?, substrate, product, ligand, target

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 5,698,401 A (FESIK et al) 16 December 1997, see entire document, especially Abstract, claim 1 and column 15 line 27 through column 18 line 60.	1-11 --- 17, 18
X --- Y	HAJDUK et al. One-Dimensional Relaxation- and Diffusion-Edited NMR Methods for Screening Compounds that Bind to Macromolecules. J. Am. Chem. Soc. 17 December 1997, Vol. 119, No. 50, pp. 12257-12261, see entire article, especially "Results and Discussion" section.	1-11 --- 17, 18
X --- Y	US 5,804,390 A (FESIK et al) 08 September 1998, see entire document, especially Abstract, claims 1-4 and columns 15-18.	1-11 --- 17, 18



Further documents are listed in the continuation of Box C.



See patent family annex.

*

Special categories of cited documents:

"A"

document defining the general state of the art which is not considered to be of particular relevance

"E"

earlier document published on or after the international filing date

"L"

document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O"

document referring to an oral disclosure, use, exhibition or other means

"P"

document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

13 DECEMBER 2000

Date of mailing of the international search report

25 JAN 2001

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

MAURIE E. GARCIA

Telephone No.

(703) 308-0196

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/26949

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-11, 17, 18

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/26949

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-11, 17 and 18, drawn to a method of identifying compounds that interact with a target molecule.

Group II, claim(s) 12 and 14-16, drawn to method of determining an interaction constant.

Group III, claim(s) 13, drawn to a method using NMR for screening.

Group IV, claim(s) 19, drawn to a second method of identifying compounds that interact with a target molecule.

The inventions listed as Groups I-IV do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Each of the groups comprises a different method and thus lacks the same or corresponding special technical feature. The methods are different because they use different steps, require different reagents and produce different products and/or results. Thus these methods have different issues and represent distinct subject matter. The particular steps of each method would be the technical feature that links the claims of each group. Since these steps are different for each of Groups I-IV, the groups lack unity.

Moreover, the method of Group I is known in the art. Fesik et al (US 5698401) discloses a method of identifying compounds that bind to a specific target using NMR experiments (see Abstract). Specifically, differences in chemical shift are measured between one or more ligands and a target before and after binding (see patented claim 1). In Example 2 of the patent (beginning in column 15), inhibitors of the enzyme stromelysin are determined using this technique.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

4

REC'D 20 NOV 2001

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PCT

Applicant's or agent's file reference P51032	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/26949	International filing date (day/month/year) 29 SEPTEMBER 2000	Priority date (day/month/year) 29 SEPTEMBER 1999
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant SMITHKLINE BEECHAM CORPORATION		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

I ☒ Basis of the report

II ☐ Priority

III ☒ Non-establishment of report with regard to novelty, inventive step or industrial applicability

IV ☐ Lack of unity of invention

V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

VI ☐ Certain documents cited

VII ☐ Certain defects in the international application

VIII ☐ Certain observations on the international application

Date of submission of the demand 01 MARCH 2001	Date of completion of this report 24 OCTOBER 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer <i>Dorthea Lawrence</i> For MAURIE E. GARCIA Telephone No. (703) 308-0196

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/26949

I. Basis of the report

1. With regard to the **elements** of the international application:*☒ the international application as originally filed☒ the description:

pages 1-19 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

☒ the claims:

pages 20-23 , as originally filed
pages NONE , as amended (together with any statement) under Article 19
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

☒ the drawings:

pages 1-6 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

☒ the sequence listing part of the description:

pages NONE , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

- ☒ the description, pages NONE
☒ the claims, Nos. NONE
☒ the drawings, sheets/fig NONE

5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

**Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/26949

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application.

☒ claims Nos. 12-16, 19

because:

☐ the said international application, or the said claim Nos. _ relate to the following subject matter which does not require international preliminary examination (*specify*).

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _ are so unclear that no meaningful opinion could be formed (*specify*).

☐ the claims, or said claims Nos. _ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 12-16, 19.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/26949

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. statement**

Novelty (N)

Claims 17, 18

YES

Claims 1-11

NO

Inventive Step (IS)

Claims NONE

YES

Claims 1-11, 17, 18

NO

Industrial Applicability (IA)

Claims 1-11, 17, 18

YES

Claims NONE

NO

2. citations and explanations (Rule 70.7)

The letter of 01 October 2001 is acknowledged. In this Response, applicant stated that the comments in the Written Opinion will not be substantively addressed at this time. Therefore, the comments below are maintained.

Claims 1-11 lack novelty under PCT Article 33(2) as being anticipated by Fesik et al (US 5,698,401) or Fesik et al (US 5,804,390).

Fesik et al ('401) discloses a method "for identifying compounds which bind to a specific target molecule" that uses two-dimensional ¹⁵N/¹H NMR (see Abstract and patented claims). Specifically the reference discloses "screening compounds using two-dimensional ¹⁵N/¹H NMR correlation spectral analysis" (see column 15, line 29 through column 18, line 43). The method of Fesik et al reads directly on the claimed method. Fesik et al teach taking a first spectrum (see for example, column 15, lines 48-55) and then mixing the test compound and the target and taking additional spectra; then comparing the results (see for example column 15, line 51 through column 16, line 41). Dissociation constants are determined using art-known techniques, see for example column 16, line 59 through column 17, line 30 of the patent. The targets of Fesik et al are biomolecules such as stromelysin (Example 2) and the DNA-binding domain of the E2 protein (column 17, lines 30-35), reading on the limitations of the instant claims 2 and 11. The test compounds of Fesik et al are in solution, reading on the limitations of instant claim 3. Fesik et al discloses using mixtures (libraries) of compounds in their method, see column 15, lines 48-55, for example.

Note that the Fesik et al (US 5,804,390) patent contains the same teachings at the same places in the patent document as the '401 patent as '390 is a divisional of '401. Also note the patented claims in '390.

Claims 1-11 lack novelty under PCT Article 33(2) as being anticipated by Hajduk et al.

Hajduk et al discloses one dimensional ¹H NMR techniques for (Continued on Supplemental Sheet.)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/26949

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

CLASSIFICATION:

The International Patent Classification (IPC) and/or the National classification are as listed below:

IPC(7): G01N 33/53, 33/557, 33/566, 33/567, 24/00; G01R 33/035 and US Cl.: 435/7.1; 436/501, 504, 517, 173; 505/844

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):

screening libraries of compounds (see Abstract). The targets of Hajduk et al are biomolecules such as the FK506 binding protein (see page 12258, 1st column) and stromelysin (see page 12259, 2nd column) reading on the limitations of the instant claims 2 and 11. The test compounds of Hajduk et al are in solution, reading on the limitations of instant claim 3. Hajduk et al discloses using mixtures (libraries) of compounds in their method, see page 12258, 1st column, for example. Specifically the reference discloses taking several spectra of compounds and target, together and separately over a period of time (see page 12258 and Figures 1 & 2). Spectra are compared (see page 12258, 2nd column) and "high affinity" ligands are determined. Thus, the method of Hajduk et al reads directly on the claimed method.

Claims 17 and 18 lack an inventive step under PCT Article 33(3) as being obvious over the prior art as applied above.

Fesik et al (US 5,698,401), Fesik et al (US 5,804,390) and Hajduk et al all teach the claimed method as set forth supra. The references lack the specific teaching of placing the compounds in a well-plate (instant claim 17) or quenching (instant claim 18). However, the use of well plates for storage of compounds was well known in the art at the time of filing. One of ordinary skill would be motivated to do so due to the ease of use of such formats. It was also well known in the art to quench certain reactions after a period of time, depending on the reaction of interest and the measurement technique. Thus, it would be well within the skill of the art to perform such a step depending on the specific reaction. One would be motivated to carry out such a step in order to monitor a reaction after a certain period of time (measure reaction progress, etc.)

Claims 1-11, 17 and 18 meet the criteria set out in PCT Article 33(4) for industrial applicability because the claimed method could be used to identify therapeutically or diagnostically active compounds.

----- NEW CITATIONS -----

NONE

PATENT COOPERATION T^RATY

From the INTERNATIONAL SEARCHING AUTHORITY

To: EDWARD R. GIMMI
SMITHKLINE BEECHAM CORPORATION
CORPORATE INTELLECTUAL PROPERTY, UW2220
709 SWEDELAND ROAD, P.O. BOX 1539
KING OF PRUSSIA, PA 19406-0939

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

Date of Mailing
(day/month/year) **25 JAN 2001**

Applicant's or agent's file reference
P51032

FOR FURTHER ACTION See paragraphs 1 and 4 below

International application No.
PCT/US00/26949

International filing date
(day/month/year)
29 SEPTEMBER 2000

Applicant
SMITHKLINE BEECHAM CORPORATION

1. ☒ The applicant is hereby notified that the international search report has been established and is transmitted herewith.
Filing of amendments and statement under Article 19:
 The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):
When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompanying sheet.
Where? Directly to the International Bureau of WIPO
 34, chemin des Colombettes
 1211 Geneva 20, Switzerland
 Facsimile No.: (41-22) 740.14.35
For more detailed instructions, see the notes on the accompanying sheet.
2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.
3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:
 - ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
 - ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.
4. **Further action(s):** The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 bis 1 and 90 bis 3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231
Facsimile No. (703) 305-3230

Authorized officer

MAURIE E. GARCIA
Dorothea Lawrence
Telephone No. (703) 308-0196

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference P51032	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/US00/26949	International filing date (day/month/year) 29 SEPTEMBER 2000	(Earliest) Priority Date (day/month/year) 29 SEPTEMBER 1999
Applicant SMITHKLINE BEECHAM CORPORATION		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:
- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.
2. ☐ Certain claims were found unsearchable (See Box I).
3. ☒ Unity of invention is lacking (See Box II).
4. With regard to the **title**,
- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established by this Authority to read as follows:
5. With regard to the **abstract**,
- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.
6. The figure of the drawings to be published with the abstract is Figure No. _____
- ☐ as suggested by the applicant.
- ☐ because the applicant failed to suggest a figure.
- ☐ because this figure better characterizes the invention.
- ☒ None of the figures.

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims: it is covered by claims Nos.:
1-11, 17, 18

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/26949

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : G01N 33/53, 33/557, 33/566, 33/567, 24/00; G01R 33/035

US CL : 435/7.1; 436/501, 504, 517, 173; 505/844

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/7.1; 436/501, 504, 517, 173; 505/844

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WEST, STN (CAPLUS, SciSearch)

Terms: NMR, nuclear magnetic resonance, one/two dimensional (1D, 2D), screen?, interact, bind?, substrate, product, ligand, target

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 5,698,401 A (FESIK et al) 16 December 1997, see entire document, especially Abstract, claim 1 and column 15 line 27 through column 18 line 60.	1-11 --- 17, 18
X --- Y	HAJDUK et al. One-Dimensional Relaxation- and Diffusion-Edited NMR Methods for Screening Compounds that Bind to Macromolecules. J. Am. Chem. Soc. 17 December 1997, Vol. 119, No. 50, pp. 12257-12261, see entire article, especially "Results and Discussion" section.	1-11 --- 17, 18
X --- Y	US 5,804,390 A (FESIK et al) 08 September 1998, see entire document, especially Abstract, claims 1-4 and columns 15-18.	1-11 --- 17, 18

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
A document defining the general state of the art which is not considered to be of particular relevance	*N* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
E earlier document published on or after the international filing date	*Y* document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*X* document member of the same patent family
O document referring to an oral disclosure, use, exhibition or other means	
P document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

13 DECEMBER 2000

Date of mailing of the international search report

25 JAN 2001

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

MAURIE E. GARCIA

Telephone No. (703) 308-0196

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

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Group III, claim(s) 13, drawn to a method using NMR for screening.

Group IV, claim(s) 19, drawn to a second method of identifying compounds that interact with a target molecule.

The inventions listed as Groups I-IV do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Each of the groups comprises a different method and thus lacks the same or corresponding special technical feature. The methods are different because they use different steps, require different reagents and produce different products and/or results. Thus these methods have different issues and represent distinct subject matter. The particular steps of each method would be the technical feature that links the claims of each group. Since these steps are different for each of Groups I-IV, the groups lack unity.

Moreover, the method of Group I is known in the art. Fesik et al (US 5698401) discloses a method of identifying compounds that bind to a specific target using NMR experiments (see Abstract). Specifically, differences in chemical shift are measured between one or more ligands and a target before and after binding (see patented claim 1). In Example 2 of the patent (beginning in column 15), inhibitors of the enzyme stromelysin are determined using this technique.

NOTES TO FORM PCT/ISA/220 (continued)

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under Article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

The statement should be brief, it should not exceed 500 words if in English or if translated into English:

It should not be confounded with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It should not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

In what language ?

The amendments must be made in the language in which the international application is published. The letter and any statement accompanying the amendments must be in the same language as the international application if that language is English or French; otherwise, it must be in English or French, at the choice of the applicant.

Consequence if a demand for international preliminary examination has already been filed ?

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase ?

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.